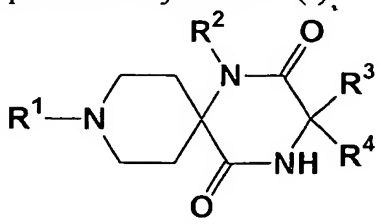
CLAIMS

1. A compound represented by formula (I),



(I)

wherein R^1 represents (1) ring 1, or (2) C1-8 alkyl, C2-4 alkenyl or C2-4 alkynyl optionally substituted with 1-3 substituents selected from the following (a)-(i): (a) $-OR^5$, (b) $-COR^6$, (c) $-NR^7R^8$, (d) $-CONR^9R^{10}$, (e) $-NR^{11}COR^{12}$, (f) $-NR^{13}SO_2R^{14}$, (g) ring 1, (h) $=NR^{15}$, (i) $=NOR^{16}$,

R^5-R^{13}, R^{15} and R^{16} each represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) ring 1, or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl optionally substituted with 1-5 substituents selected from ring 1 and -O-ring 1,

R^{14} represents C1-4 alkyl or ring 1,

ring 1 represents (1) C3-15 mono-, bi- or tri-carbocyclic aryl which may be partially or fully saturated, or (2) 3- to 15-membered mono-, bi- or tri-cyclic hetero aryl containing 1-4 nitrogen atoms, 1-2 oxygen atoms and/or 1-2 sulfur atoms which may be partially or fully saturated,

ring 1 may be substituted with 1-5 substituents selected from (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) halogen, (5) cyano, (6) ring 2, (7) $-OR^{17}$, (8) $-SR^{18}$, (9) $-NR^{19}R^{20}$, (10) $-COR^{21}$, (11) $-COOR^{22}$, (12) $-CONR^{23}R^{24}$, (13) $-NR^{25}COR^{26}$, (14) $-SO_2NR^{27}R^{28}$, (15) $-NR^{29}SO_2R^{30}$, (16) $-N(SO_2R^{31})_2$, (17) oxo, and (18) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl optionally substituted with 1-5 substituents selected from the following (a)-(e): (a) halogen, (b) ring 2, (c) $-OR^{32}$, (d) $-NR^{33}COR^{34}$, (e) $=NOR^{35}$,

R^{17}-R^{29} and R^{32}-R^{35} each represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) ring 2, or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl optionally substituted with 1-3 substituents selected from the following (a)-(f): (a) ring 2, (b) $-OR^{36}$, (c) $-COOR^{37}$, (d) $-NR^{38}R^{39}$, (e) halogen, (f) $=NR^{40}$,

R^{30} and R^{31} each represents C1-4 alkyl,

R^{36}-R^{40} each represents hydrogen or C1-4 alkyl optionally substituted with hydroxyl,

ring 2 represents (1) C3-15 mono-, bi- or tri-carbocyclic aryl which may be partially or fully saturated, or (2) 3- to 15-membered mono-, bi- or tri-cyclic hetero aryl containing 1-4 nitrogen atoms, 1-2 oxygen atoms and/or 1-2 sulfur atoms which may be partially or fully saturated,

ring 2 may be substituted with 1-5 substituents selected from (1) C1-8 alkyl, (2) halogen, (3) $-OCF_3$, (4) cyano, (5) ring 3, (6) $-OR^{41}$, (7) $-NR^{42}R^{43}$, (8) $-COR^{44}$, (9) $-COOR^{45}$, (10) $-CONR^{46}R^{47}$, (11) $-NR^{48}COR^{49}$, (12) $-SO_2NR^{50}R^{51}$, (13) $-NR^{52}SO_2R^{53}$, and (14) $-C(NH_2)=NR^{54}$,

R^{41}-R^{52} and R^{54} each represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) ring 3, (6) $-OR^{55}$, or (7) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl optionally substituted with 1-3 substituents selected from the following (a)-(d): (a) ring 3, (b) $-OR^{56}$, (c) $-COOR^{57}$, (d) $-NR^{58}R^{59}$,

R^{53} represents C1-8 alkyl,

R^{55}-R^{59} each represents hydrogen or C1-4 alkyl,

ring 3 represents (1) C3-8 mono-carbocyclic aryl which may be partially or fully saturated, or (2) 3-8 membered mono-cyclic hetero aryl containing 1-4 nitrogen atoms, 1-2 oxygen atoms and/or 1-2 sulfur atoms which may be partially or fully saturated,

ring 3 may be substituted with 1-3 of =O or =S,

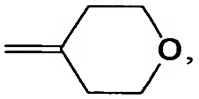
R^2 represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) ring 4, or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl optionally substituted with 1-5 substituents selected from the following (a)-(i): (a) hydrogen, (b) $-OR^{60}$, (c) $-NR^{61}R^{62}$, (d) $-CONR^{63}R^{64}$, (e) $-NR^{65}COR^{66}$, (f) $-NR^{67}SO_2R^{68}$, (g) $NR^{69}COOR^{70}$, (h) ring 4, (i) cyano,

R^{60}-R^{67} and R^{69} each represents hydrogen, C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl,

R^{68} and R^{70} each represents C1-4 alkyl, C2-4 alkenyl or C2-4 alkynyl,

ring 4 represents phenyl, pyridinyl, or C3-8 cycloalkyl,

ring 4 may be substituted with 1-5 of C1-4 alkyl,

R^3 and R^4 together with a carbon atom to which they are attached, form C3-8 cycloalkyl, or R^3 and R^4 each represents (1) hydrogen, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl optionally substituted with 1-5 substituents selected from the following (a)-(c): (a) ring 5, (b) hydroxyl, (c)  ,

ring 5 represents (1) C3-15 mono-, bi- or tri-carbocyclic aryl which may be partially or fully saturated, or (2) 3- to 15-membered mono-, bi- or tri-cyclic hetero aryl containing 1-4 nitrogen atoms, 1-2 oxygen atoms and/or 1-2 sulfur atoms which may be partially or fully saturated,

ring 5 may be substituted with 1-5 of $-OR^{71}$, C1-4 alkyl or oxo,

R^{71} represents hydrogen or C1-4 alkyl,

a quaternary ammonium salt thereof, an N-oxide thereof, or a salt thereof.

2. The compound according to claim 1, which is selected from the group consisting of

(1) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-methylaminocarbonyl-2-chlorophenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(2) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-(5-oxo-4,5-dihydro-1,2,4-thiadiazol-3-yl)phenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(3) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-2-ethylbutyl)-9-(4-(4-(2-methoxyethylaminocarbonyl)-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(4) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-2-methylpropyl)-9-(4-(4-methylsulfonylamino-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(5) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-(pyrrolidin-1-yl)carbonyl-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(6) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-2-ethylbutyl)-9-(4-(2-methoxy-4-methylsulfonylaminophenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(7) (3S)-1-butyl-2,5-dioxo-3-(2-methylpropyl)-9-(4-(2-methoxy-4-methylsulfonylaminophenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(8) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-(2-methylpropyl)carbonylaminophenylmethyl)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(9) (3R)-1-butyl-2,5-dioxo-3((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-(2-methylpropyl)carbonylamino-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(10) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(2-(4-methylaminocarbonylphenoxy)ethyl)-1,4,9-triazaspiro[5.5]undecane,

(11) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(5-(4-methylaminocarbonylphenoxy)pentyl)-1,4,9-triazaspiro[5.5]undecane,

(12) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-methylaminocarbonylphenoxy)butyl)-1,4,9-triazaspiro[5.5]undecane,

(13) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(cyclohexen-4-yl)methyl)-9-(4-(4-methylaminocarbonylphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(14) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-methylsulfonylaminophenoxy)butyl)-1,4,9-triazaspiro[5.5]undecane, and

(15) (3R)-1-pentyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-methylaminocarbonylphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane.

3. The compound according to claim 1, which is selected from the group consisting of

(1) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-cyclopropylmethylaminocarbonylphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(2) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-carboxy-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(3) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-methylaminocarbonyl-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(4) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-carboxy-2-methoxyphenylmethyl)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(5) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-(N,N,-dimethylaminocarbonyl)-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(6) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-carboxy-2-ethoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(7) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-carboxy-2,6-dimethylphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(8) (3R)-1-pentyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-carboxy-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(9) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-2-ethylbutyl)-9-(4-(4-carboxy-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(10) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-cyclopropylmethylaminocarbonylphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(11) (3R)-1-propyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-dimethylaminocarbonyl-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(12) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cycloheptylmethyl)-9-(4-(4-carboxy-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(13) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclopentylmethyl)-9-(4-(4-carboxy-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(14) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclopentylmethyl)-9-(4-(4-carboxy-2-ethoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(15) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-cyclopropylmethylaminocarbonyl-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(16) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-methylaminocarbonyl-2-methoxyphenylmethyl)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(17) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-isopropylaminocarbonyl-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,

(18) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-(2-methylpropyl)aminocarbonyl-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
(19) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-(2,2-dimethylpropylaminocarbonyl)-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
(20) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-isopropylcarbonylaminophenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
(21) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-(2-methylpropyl)carbonylaminophenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
(22) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(tetrahydropyran-4-yl)methyl)-9-(4-(4-isopropylcarbonylamino-2-methoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
(23) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(cyclopenten-4-yl)methyl)-9-(4-(4-carboxy-2-methylphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
(24) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-(cyclopenten-4-yl)methyl)-9-(4-(4-carboxy-2-ethoxyphenoxy)phenylmethyl)-1,4,9-triazaspiro[5.5]undecane,
(25) (3R)-1-(2-butynyl)-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(4-(4-methylaminocarbonylphenoxy)butyl)-1,4,9-triazaspiro[5.5]undecane,
(26) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(1-(4-(4-methylaminocarbonylphenoxy)phenyl)ethyl)-1,4,9-triazaspiro[5.5]undecane, and
(27) (3R)-1-butyl-2,5-dioxo-3-((1R)-1-hydroxy-1-cyclohexylmethyl)-9-(1-(4-(4-carboxyphenoxy)phenyl)ethyl)-1,4,9-triazaspiro[5.5]undecane.

4. The compound according to claim 1, wherein R^1 is C1-8 alkyl, C2-4 alkenyl, or C2-4 alkynyl substituted with $-COR^6$, $=NR^{15}$, or $=NOR^{16}$, in which R^6, R^{15} and R^{16} have the same meanings as defined in claim 1.

5. The compound according to claim 1, wherein at least one of substituents of ring 1 in R^1 is $-COR^{12}$, oxo, or $=NOR^{35}$, in which R^{12} and R^{35} have the same meanings as defined in claim 1.

6. The compound according to claim 1, wherein at least one of substituents of ring 2 in R^1 is $-COR^{44}$ or $-C(NH_2)=NOR^{54}$, in which R^{44} and R^{54} have the same meanings as defined in claim 1.

7. The compound according to claim 1, wherein at least one of substituents of ring 3 in R^1 is =O or =S.

8. A pharmaceutical composition which comprises, as an active ingredient, the compound represented by formula (I) according to claim 1, a quaternary ammonium salt thereof, an N-oxide thereof, or a salt thereof.

9. A regulator of a chemokine/chemokine receptor, which comprises, as an active ingredient, the compound represented by formula (I) according to claim 1, a quaternary ammonium salt thereof, an N-oxide thereof, or a salt thereof.

10. The regulator of a chemokine/chemokine receptor according to claim 9, which is a CCR5 antagonist.

11. A pharmaceutical composition for prevention and/or treatment for inflammatory diseases, immunologic diseases, human immunodeficiency virus, allergic diseases, ischemia-reperfusion injury, acute respiratory distress syndrome, shock accompanied by bacterial infection, diabetes mellitus, or metastasis, which comprises, as an active ingredient, the compound represented by formula (I) according to claim 1, a quaternary ammonium salt thereof, an N-oxide thereof, or a salt.

12. A method for antagonizing CCR5 in a mammal, which comprises administering to a mammal an effective amount of the compound of formula (I) according to claim 1, a quaternary ammonium salt thereof, an N-oxide thereof, or a salt thereof.

13. Use of the compound of formula (I) according to claim 1, a quaternary ammonium salt thereof, an N-oxide thereof, or a salt thereof for the manufacture of a CCR5 antagonist.